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Application Number	09/971,774
Filing Date	October 9, 2001
First Named Inventor	REDMOND
Examiner Name	Maier, Leigh C.
Group Art Unit	1623

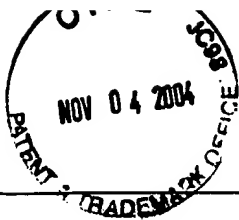
Total Number of Pages in This Submission	Attorney Docket Number	1194-180
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REMARKS:

SUBMITTED BY		Complete (if applicable)			
NAME AND REG. NUMBER	Willem F. DeWeerd, Reg. No. 51,613				
SIGNATURE		DATE	November 4, 2004	DEPOSIT ACCOUNT USER ID 02-2135	XXX



<b>IN THE UNITED STATES PATENT AND TRADEMARK OFFICE</b>	Application Number	<b>09/971,774</b>
	Filing Date	<b>October 9, 2001</b>
	First Named Inventor	<b>REDMOND</b>
	Group Art Unit	<b>1623</b>
	Examiner Name	<b>Maier, Leigh C.</b>
	Attorney Docket Number	<b>1194-180</b>
Title: <b>USE OF TAUROLIDINE AND/OR TAURULTAM FOR TREATMENT OF ABDOMINAL CANCER AND/OR FOR PREVENTION OF METASTASES</b>		

**APPEAL BRIEF**

Mail Stop - Appeal Brief-Patents  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1540

Dear Sir:

This is an appeal from the Office Action dated April 6, 2004 in which claims 1-12, and 26 were rejected. A Notice of Appeal was filed on August 4, 2004, together with an Amendment and Claim for Foreign Priority. An Advisory Action was mailed on September 24, 2004, wherein the proposed amendments to the specification and the claim to foreign priority were entered for purposes of the appeal. However, the amendment did not overcome the final rejection which was maintained.

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### **Real Party in Interest**

The owner of the above-referenced patent application and the real party in interest in this appeal is the assignee, Ed. Geistlich & Soehne AG fuer Chemische Industrie, located in Switzerland.

### **Related Appeals and Interferences**

Applicants are unaware of any other appeals or interferences related to the subject matter of this appeal.

### **Status of Claims**

Claims 1-12, and 26 are pending and are under final rejection as a result of the Office Action dated April 6, 2004 claims 13-25 were cancelled without prejudice. Applicants appeal from the rejection of claims 1-12, and 26. The appealed claims are reproduced in the appendix.

### **Status of Amendments**

Applicants filed an Amendment and Claim for Foreign Priority together with a Notice of Appeal in response to the Office Action dated April 6, 2004. In the amendment the specification was amended to properly claim foreign priority to GB 97 16219.2, filed July 31, 1997. In the Advisory Action dated September 24, 2004 the Examiner entered the amendment for purposes of the Appeal.

### **Summary of the Claimed Subject Matter**

The invention is directed to a method of treating abdominal cancer comprising performing a surgery on a patient's abdomen by forming a surgical opening in said patient's abdomen, surgically removing a cancerous tumor from the patient's abdomen through the surgical opening, and closing said surgical opening. The method includes a step of administering

taurolidine, taurultam or a mixture thereof to the patient's abdomen prior to closing of the surgical opening for removing a cancerous tumor and after surgically removing said cancerous tumor. The claimed invention thus requires all the steps of: 1) forming a surgical opening in a patient's abdomen; 2) surgically removing a cancerous tumor from the patient's abdomen through the surgical opening; 3) administering taurolidine, taurultam or a mixture thereof to the patient's abdomen prior to closing of the surgical opening and after surgically removing the cancerous tumor; 4) closing the surgical opening; and 5) additionally administering taurolidine, taurultam or a mixture thereof to the patient after closing the surgical opening.

In addition, the administration of taurolidine, taurultam or a mixture thereof to the patient may be either intravenously or through installation as set forth in dependent claim 2. Further, direct administration to the abdomen of the patient of taurolidine, taurultam or a mixture thereof may be through a trocar tube, which trocar is also used for the surgical steps of removing the tumor, as set forth in dependent claims 5 and 6. Furthermore, administration of the aforementioned compounds to a patient may be prior to surgery as in dependent claims 3, 4, and 10, or in combination with other pharmaceutical compounds such as heparin and 5-fluorouracil as set forth in dependent claims 9 and 26.

An important aspect of the abdominal cancer treatment method of the current invention is to improve treatment and survival of patients with abdominal cancer. Such an improvement can be established by removing the cancer through surgery of the abdomen and at the same time, either prior, after or both prior and after completion of the surgery, administering taurolidine, taurultam or a mixture thereof to the patient. The method of treatment of abdominal cancer according to the current invention allows for improved recovery and survival of the patient as is

shown for example in the specification in example 6 were a reduction of angiogenic growth factors was observed following treatment of patients according to the method of the invention. (Specification on page 13, lines 1-23)

The invention therefore comprises a method for the treatment of abdominal cancer including performing a surgery in the abdomen of a patient thereby removing an abdominal cancer and administering taurolidine, taurultam or a mixture thereof to the patient, as set forth in claims 1-12, and 26. Specifically, independent claim 1 requires administering the taurolidine, taurultam or a mixture thereof into the patient both prior to closing the surgical opening from which the abdominal tumor was removed as well as after closing of said surgical opening.

#### **Grounds of Rejection to be Reviewed on Appeal**

The following grounds of rejection are to be reviewed by this appeal:

1) Whether the subject matter of claims 1-5, 8, 9, 11, and 12 is non-obvious over Jacobi et al. (Langenbecks Arch. Cir., 1997) in view of Monson et al. (WO 92/00743) under by 35 U.S.C. 103(a).

2) Whether the subject matter of claims 1-12 is non-obvious over Jacobi et al (Langenbecks Arch. Cir., 1997) in view of Monson et al (WO 92/00743) and further in view of U.S. Patent No. 5,176,651 (Allgood et al) under 35 U.S.C. 103(a).

3) Whether the subject matter of claims 1-5, 8, 9, 11, and 12 is non-obvious over Jacobi et al (Langenbecks Arch. Cir., 1997) in view of Monson et al (WO 92/00743) and further in view of U.S. Patent No. 5,262,403 (Nicolson et al) under 35 U.S.C. 103(a).

4) Whether the subject matter of claims 1-5, 8, 9, 11, 12, and 26 is non-obvious over Jacobi et al (Langenbecks Arch. Cir., 1997) in view of Monson et al (WO 92/00743) and further in view of Physicians Desk Reference (PDR - 1995) under 35 U.S.C. 103(a).

### **Arguments**

#### **1. Claims 1-5, 8, 9, 11, and 12 are non-obvious over Jacobi et al. in view of Monson et al.**

According to the Examiner applicants contention that Jacobi et al does not teach each and every step of the present invention is not a persuasive argument in view of the fact that the rejection of the claims is one of obviousness. Further, the Examiner has asserted that it would have been obvious to one of ordinary skill in the art to administer a solution of taurolidine and/or taurultam during laparoscopic cancer surgery because Jacobi et al had taught that the intraperitoneal administration of taurolidine or a combination of taurolidine and heparin at the time of laparoscopic surgery for tumor removal reduces the incidence of tumor growth and trocar metastases. According to the Examiner, Monson et al had taught the taurolidine and taurultam are functional equivalents for the inhibition of metastases. Therefore, the Examiner asserted that in the absence of unexpected results, one of ordinary skill in the art would reasonably expect success in the use of taurolidne and/or taurultam in the procedure of administering these compounds before and/or after cancer surgery for all of the recited cancers, and would optimize a solution concentration with routine experimentation, and select any common type of administration, such as IV or catherization.

In addition, the Examiner asserted, in response to Applicants' argument that the Examiner's reasoning is hindsight, that as long as the reasoning applied takes into account only

knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the Applicants' disclosure, such reasoning is proper. Therefore, according to the Examiner, Applicants' argument that both Jacobi et al do not teach each and every step of the present claims and that the Examiner applied hindsight reasoning was non-persuasive in overcoming the rejection of the claims.

In contrast to the Examiner's assertions, the Jacobi et al reference does not teach or suggest all of forming a surgical opening in a patient's abdomen, surgically removing a cancerous tumor from the patient's abdomen through the surgical opening, administering taurolidine, taurultam or a mixture thereof to the patient's abdomen prior to closing of the surgical opening and after surgically removing the cancerous tumor, closing the surgical opening, and additionally administering taurolidine, taurultam or a mixture thereof to the patient after closing the surgical opening. In order to render claims obvious, a combination of prior art must at least suggest the elements of the claims. In the present case, all of the claims of the present applications specifically require all the above mentioned steps. In the present case, the applied prior art of Jacobi et al and Monson et al cannot be combined to suggest the particular combination of elements set forth above.

While Jacobi et al. applied postoperative lavage with taurolidine in subjects undergoing laparoscopic resection of malignancies, there is no teaching or suggestion whatsoever in Jacobi et al. of the specific steps of the present claims, wherein the tumor is removed, taurolidine and/or taurultam is administered to the abdomen prior to closing of the surgical opening and after surgical removal of the tumor, and additionally administering taurolidine and/or taurultam to the patient after closing the surgical opening. In fact, the Jacobi et al. reference merely discloses in

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vivo experiments in animals, according to the following steps of 1) introducing cancer cells intraperitoneally into each animal through abdominal incisions, 2) establishing pneumoperitoneum in each animal utilizing a gas, after introduction of the cancer cells, 3) introducing intraperitoneally a solution containing taurolidine, 4) closing abdominal incisions, and 5) excising later intraperitoneal tumors after the animals were sacrificed. Further, Monson et al. merely discloses the administration of taurolidine or taurultam by injection or infusion for the prevention of cancer metastases. Absent hindsight knowledge of the present claims, Jacobi et al. and Monson et al. cannot be combined to suggest the specific sequence of steps set forth above.

Therefore, the applied prior art does not suggest the series of steps set forth above and required by all of the present claims. In contrast with the present claims, Jacobi et al. experimentally introduce cancer cells to an animal, then apply taurolidine, and later remove tumors. With patients, Jacobi et al. merely apply postoperative lavage with taurolidine in patients undergoing open and laparoscopic resection of malignancies. There is no suggestion in the applied prior art of the specific steps of the present claims, wherein the tumor is removed, taurolidine and/or taurultam is administered to the abdomen prior to closing of the surgical opening and after surgical removal of the tumor, and additionally administering taurolidine and/or taurultam to the patient after closing the surgical opening.

Furthermore, with respect to claims 3, 4 and 10, which further specify additionally administering taurolidine and/or taurultam to the patient prior to forming the surgical opening in the patient's abdomen, no combination of the cited references suggest this embodiment of the invention.

Thus, the claimed invention in claims 1-5, 8, 9, 11, and 12 is unobvious over Jacobi et al.



in view of Monson et al., as the Jacobi et al. reference does not teach or suggest the required steps in treating a patient with abdominal cancer according to the current invention as described above and combining Monson et al. with Jacobi et al does not cure this manifest deficiency for the reasons set forth above.

Applicants thus respectfully submit that the claims 1-5, 8, 9, 11, and 12 of the present application are not obvious over Jacobi et al. in view of Monson et al., and applicants respectfully request withdrawal of this rejection.

**2. Claims 1-12 are non-obvious over Jacobi et al in view of Monson et al and further in view of Allgood et al.**

The Examiner applies the same reasoning with respect to his rejection over Jacobi et al in view of Monson et al and asserts that applicants do not provide any reasoning of why Allgood et al, disclosing a combination surgical trocar housing and selective reducing sleeve, cannot be combined with Jacobi et al and Monson et al. Therefore, the Examiner asserts that, as Allgood et al was cited for a specific teaching that allowed its combination with Jacobi et al and Monson et al, applicants response to the rejection of obviousness was not persuasive.

Allgood et al. merely discusses endoscopic surgery, but cannot be combined with Jacobi et al. and Monson et al. to suggest the specific sequence of steps set forth in the claims, as outlined above. Furthermore, with respect to claim 6, which further specifies passing a solution containing taurolidine and/or taurultam through a trocar to so as to contact internal tissue of the patient with the solution, no combination of the cited references suggest this embodiment of the

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invention. In contrast to the trocar in claim 6, the disclosure in Allgood et al, includes the description of a sealing means in the trocar to prevent the flow of fluid.

Thus, the claimed invention in claims 1-12 is unobvious over Jacobi et al. in view of Monson et al. in further view of Allgood et al, as the Jacobi et al. reference does not teach or suggest the required steps in treating a patient with abdominal cancer according to the current invention as described above and combining Monson et al. and Allgood et al with Jacobi et al does not cure this manifest deficiency for reasons set forth above.

Applicants thus respectfully submit that the claims 1-12 of the present application are not obvious over Jacobi et al. in view of Monson et al. in further view of Allgood et al, and applicants respectfully request withdrawal of this rejection.

**3) Claims 1-5, 8, 9, 11, and 12 are non-obvious over Jacobi et al in view of Monson et al and further in view of Nicholson et al.**

The Examiner applies the same reasoning with respect to his rejection over Jacobi et al in view of Monson et al and asserts that applicants do not provide any reasoning of why Nicholson et al, disclosing glycosaminoglycan derivatives and their use as inhibitors of tumor invasiveness of metastatic profusion, cannot be combined with Jacobi et al and Monson et al. Therefore, the Examiner asserts that, as Nicholson et al was cited for a specific teaching that allowed its combination with Jacobi et al and Monson et al, applicants response to the rejection of obviousness was not persuasive.

Nicolson et al. merely discloses the use of glycosaminoglycans in a method for impeding the formation of tumor metastasis or tumor invasiveness in a host, but cannot be combined with Jacobi et al. and Monson et al. to suggest the specific sequence of claim features set forth above.

Thus, the claimed invention in claims 1-5, 8, 9, 11, and 12 is unobvious over Jacobi et al. in view of Monson et al. in further view of Nicholson et al, as the Jacobi et al. reference does not teach or suggest the required steps in treating a patient with abdominal cancer according to the current invention as described above and combining Monson et al. and Nicholson et al with Jacobi et al does not cure this manifest deficiency for reasons set forth above.

Applicants thus respectfully submit that the claims 1-5, 8, 9, 11, and 12 of the present application are not obvious over Jacobi et al. in view of Monson et al. in further view of Nicholson et al, and applicants respectfully request withdrawal of this rejection.

**4) Claims 1-5, 8, 9, 11, 12, and 26 are non-obvious over Jacobi et al in view of Monson et al and further in view of Physicians Desk Reference (PDR - 1995).**

The Examiner applies the same reasoning with respect to his rejection over Jacobi et al in view of Monson et al and asserts that applicants does not provide any reasoning of why the PDR-1995, disclosing the use of 5-fluorouracil, cannot be combined with Jacobi et al and Monson et al. Therefore, the Examiner asserts that, as the PDR-1995 was cited for a specific teaching that allowed its combination with Jacobi et al and Monson et al, applicants response to the rejection of obviousness was not persuasive.

In addition to Jacobi et al and Monson et al the PDR-1995 discloses merely the effective

use 5-FU in the treatment of various cancers but cannot be combined with Jacobi et al. and Monson et al. to suggest the specific sequence of claim features outlined above.

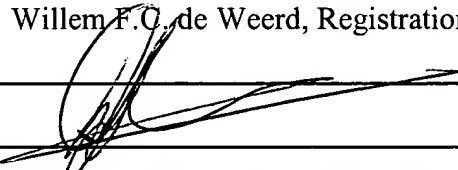
Thus, the claimed invention in claims 1-5, 8, 9, 11, 12 and 26 is unobvious over Jacobi et al. in view of Monson et al. in further view of PDR-1995, as the Jacobi et al. reference does not teach or suggest the required steps in treating a patient with abdominal cancer according to the current invention as described above and combining Monson et al. and PDR-1995 with Jacobi et al does not cure this manifest deficiency for reasons set forth above.

Applicants thus respectfully submit that the claims 1-5, 8, 9, 11, 12, and 26 of the present application are not obvious over Jacobi et al. in view of Monson et al. in further view of PDR-1995, and applicants respectfully request withdrawal of this rejection

**CONCLUSION**

None of the applied references can be combined to suggest the specific steps of the present claims, wherein a tumor is removed, taurolidine and/or taurultam is administered to the abdomen prior to closing of the surgical opening and after surgical removal of the tumor, and additionally administering taurolidine and/or taurultam to the patient after closing the surgical opening. Thus, in view of the above, the claims of the current invention are non-obvious over Jacobi et al. in combination with the other applied art.

In view of the foregoing, Applicants respectfully submit that claims 1-12, and 26 are non-obvious over the cited prior art under 35 U.S.C. 103(a). All of the grounds for the rejections of claims 1-12, and 26 as advanced by the Examiner are submitted to be unsupportable by the record, and thus improper. The Honorable Board is therefore respectfully requested to reverse the final rejection, and to direct the passage of this application to issue.

<b>RESPECTFULLY SUBMITTED,</b>					
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## APPENDIX

1. A method of treating abdominal cancer comprising performing a surgery on a patient's abdomen by forming a surgical opening in said patient's abdomen, surgically removing a cancerous tumor from the patient's abdomen through the surgical opening, and closing said surgical opening, the method including a step of administering taurolidine, taurultam or a mixture thereof to the patient's abdomen prior to said closing of said surgical opening and after said surgically removing said cancerous tumor, so as to treat cancer in the patient's abdomen, further including a step of additionally administering taurolidine, taurultam or a mixture thereof to said patient after said closing said surgical opening.

2. The method of claim 1 wherein, after closing said surgical opening, said taurolidine, taurultam or mixture thereof is administered to said patient by installation or intravenous infusion.

3. The method of claim 2 wherein, further including the step of additionally administering taurolidine, taurultam or a mixture thereof to said patient prior to forming said surgical opening in said patient's abdomen.

4. The method of claim 1, further including the step of additionally administering taurolidine, taurultam or a mixture thereof to said patient prior to forming said surgical opening in said patient's abdomen.

5. The method of claim 1, wherein performing said surgery on said patient includes introducing a trocar tube into said patient during laparoscopic tumor surgery so as to conduct laparoscopic tumor surgery so as to conduct laparoscopic tumor surgery utilizing said trocar tube.

6. The method of claim 5 wherein during said surgery, said administering said taurolidine, taurultam or mixture thereof to said patient's abdomen is conducted by passing a solution containing said taurolidine, taurultam or mixture thereof through said trocar tube so as to contact internal tissue of the patient with said solution.

7. The method of claim 6 further comprising the step of withdrawing said trocar from said patient prior to said closing said surgical opening and prior to said step of additionally administering said taurolidine, taurultam or mixture thereof to said patient after closing said surgical opening.

8. The method of claim 1 wherein said taurolidine, taurultam or a mixture thereof is present in a solution containing from 0.5 to 3% by weight said taurolidine or from 2 to 3% by weight said taurultam, or a mixture thereof.

9. The method of claim 8 wherein said solution further contains heparin, a heparin derivative or hyaluronic acid.

10. The method of claim 6 further comprising the step of additionally introducing said solution into said patient prior to said laparoscopic tumor surgery and prior to introducing said trocar tube into said patient.

11. The method of claim 5 wherein said cancerous tumor is selected from the group consisting of oesophagus carcinoma, cardiacarcinoma, malignant degenerative ulcer, stomach carcinoma, antrum carcinoma, corpus carcinoma, align adenoma of island cells, gall duct carcinoma, distal choledochus carcinoma, pancreas head carcinoma, pancreas papilla carcinoma, pancreas corpus carcinoma, pancreas cauda carcinoma, small intestinal tract carcinoma, large intestinal tract carcinoma, sarcoma, colon malignancy, adeno carcinoma, lymphoma, malign carcinoid, melanoma, rectal carcinoma, ovarial carcinoma, mamma carcinoma, and prostate carcinoma.

12. The method of claim 1 wherein said cancerous tumor is selected from the group consisting of colon cancer, rectal cancer, pancreatic cancer, stomach cancer and lung cancer.

26. The method of claim 1 further comprising administering to said patient 5-fluorouracil (5-FU) at a dosage within a range of about 0.1-1,000 mg.